Epicardial ST Depression in Acute Myocardial Infarction

Danshi Li, Chuan Yong Li, Ah Chot Yong, Peter R. Johnston, David Kilpatrick

Abstract—The presence of electrocardiographic ST depression in acute infarction remains controversial and poorly explained. A combined animal and modeling study was performed to evaluate the source of ST changes in acute infarction. In anaesthetized sheep, small infarcts showed uniform ST elevation over the infarction whereas larger infarcts showed marked ST depression over the normal myocardium in addition to the ST elevation. These findings were replicated by bidomain models of the heart. A hollow sphere was used to model a gradually increasing infarct, and this showed that there was a decrease in the ratio of ST elevation to ST depression as the infarct was increased. The current flowing out of the heart must be identical to the current flowing back into the heart. This means that any infarction will produce ST depression as well as ST elevation, the ratio between the two being related to the size of the infarction. Small infarction is associated with a small region of ST elevation and minor ST depression of the remaining myocardium, and as the infarct region increases, the amplitude of the epicardial ST elevation falls and the amplitude of the ST depression increases. Infarction size is proportional to both the height of the ST depression on the epicardium and the strength of the epicardial ST segment dipole. (Circ Res. 1999;85:959–964.)

Key Words: electrocardiography ■ epicardial potential ■ acute infarction ■ bidomain model ■ ST depression

The origins and significance of ST depression associated with acute myocardial infarction are poorly understood and controversial.1–8 As part of a study looking at partial-thickness ischemia in an experimental animal model,9 we observed that ST depression accompanied some episodes of full-thickness ischemia and not others. The literature reflecting experimental infarction has shown that full-thickness ischemia was associated with a region of epicardial ST elevation over the ischemia with minimal changes elsewhere.10–16 This discrepancy between clinical observation and experimental results has been more fully evaluated by detailed epicardial, endocardial, and body surface ECG mapping of acute infarction in different territories and of different sizes in an experimental sheep model. The electrical changes were correlated with regional blood flow measured by fluorescent microspheres. To explain the results of the experimental infarction, we have developed several levels of a bidomain model based on that described by Tung,17 including a hollow thick-walled sphere, and a finite element model of the heart that replicated the experimental observations.

Materials and Methods

Experimental Animals

A total of 33 sheep were randomized into three groups. Transmural ischemia was achieved by completely ligating the obtuse marginal branch (OM) in group 1, the proximal left circumflex coronary artery (LCX) in group 2, and the proximal left anterior descending coronary artery (LAD) in group 3 for a minimum of 20 minutes. The epicardial ST potential fields were recorded at 1, 2, 5, 10, 15, and 20 minutes for a period of 2 seconds, respectively. The regional myocardial blood flow (RMBF) was measured before and 20 minutes after the artery was occluded. In 10 animals of groups 1 and 3, the endocardial and the epicardial potential fields were also recorded simultaneously. The left ventricular pressure, the left atrial pressure, the coronary artery flow, and lead II of the ECG were also monitored before and during ischemia. The details of the surgical procedures have been published previously.9 The investigation conforms with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1985). The RMBF was measured before ischemia and at 20 minutes of ischemia using fluorescent microspheres (Molecular Probes) as previously described.9,18

Potential Recording, Construction of Isopotential Maps, and Map Display

Epicardial potentials were recorded using an epicardial sock containing 64 electrodes (Cardiovascular Research and Training Institute, the University of Utah). Endocardial electrograms were recorded using a homemade 40-electrode basket mapping apparatus.9

Computer Modeling

Bidomain Model

The myocardium was represented by the bidomain model, in which intracavitary and extracavitary volumes occupy the same space and were separated everywhere by the membrane.

Hollow Thick-Walled Sphere

Consider two concentric spheres as a model of the left ventricle and its surrounding myocardium (Figure 1). The inner sphere, of radius $r_i$, contains the blood mass and the region between the inner sphere, and the outer sphere, of radius $r_o$, represents the cardiac muscle. In terms of a spherical coordinate system $(r, \theta, \phi)$, the blood mass is the region $0<r<r_i$ and the myocardium is the region $r_i<r<r_o$.

We generated a region of transmural ischemia, which is axially symmetric about the azimuthal axis of the spherical coordinate system, so that the potentials have no $\phi$ dependence. Further assume that the region of ischemia covers the region $0<\theta<\theta_i$ in the myocardium. This set of ischemic regions has been solved analytically, as shown in the online Materials and Methods (see http://www.circresaha.org).
Isolated Heart Model
The bidomain equations were also solved in a realistically shaped isolated heart. Transmural ischemia was simulated using the above model on both small and large regions of the myocardium.

An expanded Materials and Methods section is available online at http://www.circresaha.org.

Results
Experimental Infarction
Immediately after the OM ligation, the heart rate, the left ventricular systolic pressure, and the LAD flow (measured by flow probe) often increased slightly and gradually recovered to the control level after 20 minutes. No ventricular arrhythmias and conduction block were observed, and all the animals survived until the end of the experiment in this group. Immediately after the LAD or the LCX ligation, the left ventricular systolic pressure and the coronary flow to the nonischemic region increased slightly, but the left ventricular systolic pressure and the coronary flow to the nonischemic region started to drop after 2 minutes in all but 2 animals. The left ventricular end-diastolic pressure increased in all but 4 animals within 15 minutes. In 9 of 25 animals with either the LAD or the LCX ligation, ventricular fibrillation developed within 5 minutes, and the animals died within 15 minutes (no data from these 9 animals were included). Ventricular fibrillation developed within 20 minutes in 7 animals, all of which died within 30 minutes. The occurrence of ventricular fibrillation was preceded by a period of sustained (0.5 to 3 minutes) ventricular tachycardia. Nine animals survived the 30- to 60-minute observation period; however, 5 developed ventricular ectopics and nonsustained ventricular tachycardia, and one developed atrioventricular block. The animal survivals in different artery occlusions are summarized in Table 1.

### Table 1. Animal Survivals in OM, LCX, and LAD Ligations

<table>
<thead>
<tr>
<th>Vessel Ligated</th>
<th>OM</th>
<th>LCX</th>
<th>LAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>% Wt of LV</td>
<td>20±4</td>
<td>46±6*</td>
<td>52±5*</td>
</tr>
<tr>
<td>VF within 5 minutes</td>
<td>0</td>
<td>4 (33%)</td>
<td>5 (38%)</td>
</tr>
<tr>
<td>VF within 20 minutes</td>
<td>0</td>
<td>3 (25%)</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>Ventricular ectopics and nonsustained VT</td>
<td>0</td>
<td>3 (25%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>AVB</td>
<td>0</td>
<td>0</td>
<td>1 (7.6%)</td>
</tr>
<tr>
<td>30- to 60-minute survivals</td>
<td>8 (100%)</td>
<td>5 (42%)</td>
<td>4 (31%)</td>
</tr>
</tbody>
</table>

*P<0.001 vs OM ligation.

Regional Myocardial Blood Flow and Hemodynamic Response
Selected hemodynamic results and changes in the myocardial blood flow after 20 minutes of ligation of the different vessels are
presented in Table 2 and Figure 2, which show significantly different flow and hemodynamic changes with varied infarctions. Both the LCX and the LAD ligation caused a marked decrease in the flow to the infarcted regions (from 1.02±0.10 to 0.19±0.07 mL·min⁻¹·g⁻¹ in the LCX ligation, from 0.99±0.20 to 0.16±0.09 mL·min⁻¹·g⁻¹ in the LAD ligation, both P<0.001). In the noninfarcted regions, there was also a considerable decrease in RMBF (from 1.03±0.13 to 0.73±0.20 mL·min⁻¹·g⁻¹ in LCX ligation, from 0.89±0.21 to 0.64±0.22 mL·min⁻¹·g⁻¹ in LAD ligation, both P<0.05). The LCX and LAD ligations were accompanied by an increase in the left ventricular end-diastolic pressure (from 3±1 to 8±3 mm Hg in LCX ligation, from 1±4 to 6±7 mm Hg in LAD ligation, both P<0.05) and a decrease in the left ventricular systolic pressure (from 81±12 to 72±20 mm Hg in LCX ligation, from 92±11 to 69±13 mm Hg in LAD ligation, both P<0.05; Table 2). However, in the OM ligation, the flow to the noninfarcted region increased nonsignificantly (from 1.09±0.19 to 1.12±0.15 mL·min⁻¹·g⁻¹, P>0.05), although flow to the infarcted regions decreased by 62% (from 1.00±0.18 to 0.38±0.14 mL·min⁻¹·g⁻¹, P<0.001). Diastolic pressure and the left ventricular systolic pressure were unchanged during the OM ligation (Table 2).

The transmural flow distributions at 20 minutes of ischemia for the OM, the LCX, and the LAD ligations are presented in Table 3. During infarction, there were similar changes in the RMBF to each third of the myocardium in both the infarcted and noninfarcted regions; the endocardial/epicardial flow ratio remained unchanged. Figure 2 displays the spatial flow distributions of the left ventricles in different artery occlusions. It was plotted with the data of 3 animals from groups 1, 2, and 3, respectively. In OM occlusion, the flow reduction occurred only in the infarcted region (Figure 2A). In either the LCX or the LAD occlusion, however, flow to the noninfarcted region also reduced considerably (Figure 2B and 2C).

In all 3 occlusions, flow reduction to each third of the ventricular wall was similar.

Linear correlation was used to determine whether a statistically significant relation existed between the RMBF change during ischemia in the noninfarcted regions and the simultaneous measurements of the left ventricular end-diastolic pressure, the left ventricular systolic pressure, and the mean left atrial pressure. The RMBF change during ischemia in the noninfarcted regions inversely correlated to the left ventricular end-diastolic pressure (r = -0.82, P = 0.0002) and the mean left atrial pressure (r = -0.79, P = 0.0001) and directly correlated to the left ventricular systolic pressure (r = 0.82, P = 0.0001; Figure 3). During acute myocardial infarction, the RMBF changes in the noninfarcted regions were related to both the perfusion pressure and cardiac function.

**Epicardial Potential Distribution in Different Sizes of Infarction**

Representative maps of epicardial ST potential distribution from 3 typical experiments are displayed in Figure 4 and show significantly different ST alterations with each different infarcted region. Total occlusion of the OM produced a graduated but even peak of ST elevation in the ischemic center, with the magnitude decreasing toward the border. The ST segment was depressed slightly at the surrounding regions (Figure 4). The highest potential occurred between 5 and 10 minutes after the OM ligation.

Total ligation of either the LAD or the LCX produced a powerful dipole between ST elevation over the infarcted region and ST

**TABLE 3. Regional Myocardial Blood Flow (mL·min⁻¹·g⁻¹) Before and During Infarction**

<table>
<thead>
<tr>
<th></th>
<th>LAD/LCX Ligation</th>
<th>OM Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ischemic Region</td>
<td>Nonischemic Region</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Endo</td>
<td>1.15±0.18</td>
<td>0.17±0.07**</td>
</tr>
<tr>
<td>Mid</td>
<td>1.03±0.17</td>
<td>0.17±0.09**</td>
</tr>
<tr>
<td>Epi</td>
<td>0.87±0.19</td>
<td>0.16±0.08**</td>
</tr>
<tr>
<td>% of control</td>
<td>...</td>
<td>17±10</td>
</tr>
<tr>
<td>Ratio</td>
<td>1.32±0.26</td>
<td>1.13±0.35</td>
</tr>
</tbody>
</table>

Endo indicates endocardium; epi, epicardium; and mid, middle. % of control is calculated from the mean of endo, mid, and epi flow. Ratio is endocardial/epicardial flow ratio.

Mean±SD. *P<0.05, **P<0.001 vs control. OM = 6, LAD/LCX = 10.
depression over the noninfarcted region. The region of ST elevation is markedly asymmetric, with the highest amplitude at the boundary, a pattern of ST elevation quite different from that of the total occlusion of the OM (Figure 4).

**Endocardial Potential Mapping in Large Infarction Compared With Epicardial Potential Mapping**

From the endocardium, we recorded both ST elevation and ST depression during the ligation of either the LCX or the LAD. The results are shown in Figures 5 and 6 which display the simultaneous epicardial and endocardial ST potential recordings. The distribution patterns of ST changes in the endocardium are similar to those in the epicardium, except that potentials were lower in the endocardium. The changes in the amplitude of the ST potentials with time were also similar in the epicardium and the endocardium, ie, potential changes occurred within 30 seconds after the occlusion, reached their maximum within 5 to 10 minutes, and then decreased from 15 minutes onward.

**Concentric Spheres Model**

The bidomain model produced a set of curves around the circumference of the spheres that were symmetrical around the vertical axis for 8 different infarct sizes ranging from 0.2 radians, 6.36% of the total surface area, to 1.6 radians, or 50.1% of the surface area. The results are shown in Figure 7. There was a clear increase in the ratio of negative to positive potentials as the size increased. We evaluated the physical dimensions against this shift looking at ischemic region on the sphere, volume of ischemia, surface area of ischemia, and the integral of current density under positive and negative regions. There was a one-to-one correspondence between the integral of current density under positive and negative curves for all infarct sizes but no relationship for the other parameters. This implies that the set of curves is produced within the constraints of the bidomain model, which requires, as the heart does, that the overall current lost from the heart is zero.
Realistic Model

The model in Figure 8 shows that the patterns are very similar to those measured in the sheep. We chose to analyze multiple infarcts using the spheres for simplicity because the real heart model has the right ventricle over the septum, which interferes with the epicardial field, thus making comparisons more difficult.

Discussion

Experimental Results

In our experimental work, it was clear that the large ischemic regions were associated with marked ST depression over the nonischemic region whereas the small ischemic regions had minimal ST depression elsewhere. These results differed from the findings in the literature mainly because the previously reported studies were from small regions of infarction, which maintained a stable condition of the animal.

To explain our findings, we looked first to see if the normal (nonischemic) region was truly not ischemic. There was some suggestion of ischemia in the normal regions because of the reduced flow from microsphere measurement, but there was no ST elevation.
on the normal endocardium, which would be expected if there was concomitant ischemia. The overall reduction of flow was also small and unlikely to produce ischemia in its own right. That the flow was reduced was surprising and probably due to a decreased pressure gradient across the coronary bed. This observation needs further investigation in terms of possible therapeutic gains from maneuvers to increase blood flow in the nonischemic regions.

The significance of this remained unclear until the concentric spheres model was analyzed. This enabled a series of incremental infarcts to be studied, as shown in Figure 7. The results suggest that some basic balance between size of ischemia and ST elevation to ST depression ratio existed. An examination of physical factors has shown that the reason for this lies with basic physics.

The total current flowing out of the heart must flow back into the heart, and this paradigm was shown to be true in that the integral of current density over the ischemic region matches that over the normal region. This basic property of physics dictates that the overall current out of the heart must be zero; hence, all ST balances between elevation and depression are subject to this. The ST depression is part of the source, and the balance between elevation and depression is dependent on the zero line set by the requirement that the overall current from the heart is zero. In human practice, this requirement is modified by the use of the Wilson central terminal to set the reference potential.

Thus, any large infarct will have both ST elevation and ST depression generated at the ischemic boundary on the epicardium and the larger the infarct, the greater the ST depression. It must be pointed out, however, that these results apply only to the epicardial potentials not the body surface potentials. Although the body surface potentials are generated by the cardiac currents, they are sufficiently modified by the shape and conductivity of the organs within the thorax to make direct comparisons difficult.

There is support for this view from one of the few inverse transform studies carried out in humans with acute infarction. In this study, the epicardial potential distributions were derived from more than 200 patients with acute infarction. The results showed that a strong dipole on the epicardial surface predicted mortality for all patients including those with single vessel disease. At the time, no clear explanation for these results was advanced. Given the study presented here, it is clear that the dipole reflected the overall size of the infarction. Further support comes from a recent modeling study, which concluded that the source with full-thickness ischemia had both negative and positive ST components and which replicated the 12-lead appearance of angioplasty-induced ischemia.

The present study has provided an explanation for ST depression on the epicardium in patients with acute infarction. It also suggests that measurement of the negativity of the dipole on the epicardium should relate well to infarction size. Clearly, it is possible to have additional ischemia, but this will also be constrained by the need to have the overall current from the heart be zero. Thus, the presence of additional ischemia will probably increase the ST elevation as well as increasing the region of ST depression. However, it is not necessary to have ischemia other than the infarction to produce marked ST depression. It is important to remember that in electrocardiology the net current leaving the heart must always be zero.

Acknowledgments

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Materials and Methods

Experimental Animals

A total of 33 Polworth/Comback cross sheep (20-37 kg) of both sexes were used in this study. They were randomised into three groups.

Group 1: ligation of the obtuse marginal branch of the circumflex coronary artery (OM, n=8).

Group 2: ligation of the left circumflex coronary artery (LCX, n=12).

Group 3: ligation of the left anterior descending coronary artery (LAD, n=13).

Transmural ischemia was achieved by completely ligating the OM in group 1, the proximal LCX in group 2, and the proximal LAD in group 3 for a minimum of 20 minutes. Each ligation was conducted by applying an artery clip on the intended artery near its origin. Immediately after the artery ligation, the epicardial ST potential fields were recorded at 1, 2, 5, 10, 15, and 20 minutes for a period of 2 seconds respectively. The regional myocardial blood flow (RMBF) was measured before and 20 minutes after the artery was occluded. In ten animals of groups 2 and 3, the endocardial and the epicardial potential fields were also recorded simultaneously. The left ventricular pressure, the left atrial pressure, the coronary artery flow and lead II of the ECG were also monitored before and during ischemia.

Surgical Procedures

The investigation conforms with the Guide for the Care and Use of Laboratory Animals published by the US National Institute of Health (NIH Publication No. 85-23, revised 1985). Anaesthesia was induced intravenously with sodium pentobarbital (30 mg/kg) and then maintained at 3-8 mg/kg/hour throughout the experiment. The animals were artificially ventilated at a rate of 18-20/min with room air. A left thoracotomy was performed in the fourth intercostal space, and the heart was suspended in a pericardial cradle. In all the groups, the LCX and the LAD were each isolated proximally near the origin for the electromagnetic flow transducer (NARCO, Carolina Medical Inc, P.O. Box 307, 157 Industrial Drive, King, NC 27021, USA) and 10-20 mm distally for the artery occlusion. In group 1, the OM was also isolated near its origin for the artery occlusion. A cannula (PE 90) was inserted into the left atrial appendage for the microsphere injection.

Perfusion Beds and Regional Myocardial Blood Flow Measurement

The RMBF was measured before ischemia and at 20 minutes of ischemia using fluorescent microspheres (Molecular Probes, Inc., Eugene, OR, USA) as previously described. Fluorescent microsphere suspensions were mixed with 10 mL of warm blood and administered over
ten seconds via the cannula in the left atrium. The cannula was then flushed with 10 mL of saline. The reference flow was established using the electromagnetic flow transducer. After completion of the experiment, 10 mL of 0.1% methylene blue dye (Sigma) were injected into the LAD, and 10 mL of normal saline were injected simultaneously into the LCX to delineate the nonischemic and the ischemic areas respectively. The ischemic boundary was expected to be well defined due to fewer functionally significant collateral blood vessels. The left ventricle was divided into 3-4 circumferential rings from the base to the apex. The circumferential rings were then cut into sections of epicardial arc length 12 mm per piece. Sections of the myocardium were divided into the endocardial, the middle and the epicardial thirds. The dimension of each piece was approximately 12x10x3 mm. The areas supplied by the LCX and the LAD were cut into 20 pieces, and the area supplied by the OM 5 pieces on average. The average weight of each piece was 1.5 g (0.9-2.0g).

The RMBF in each sample was expressed both in absolute terms, as mL/min/g of myocardium and in relative terms as a percentage of the control flow obtained before ischemia. The endocardial/epicardial (endo/epi) flow ratio was obtained by dividing the flow to the endocardial third by the flow to the epicardial third.

**Potential Recording, Construction of Isopotential Maps and Map Display**

Epicardial potentials were recorded using an epicardial sock containing 64 electrodes (Cardiovascular Research and Training Institute, the University of Utah, USA). The arrangement of the 64 electrodes provided extensive coverage of the epicardial surface of the left and the right ventricles (Figure 1). Endocardial electrograms were recorded using a home-made 40-electrode basket mapping apparatus. The apparatus was oval-shaped and constructed with springy steel wire (0.25 mm in diameter) as the skeleton, and polyethylene tube (1.27 mm in outer diameter) as the outer covering, on which 40 silver electrodes were mounted. The steel skeleton consisted of 8 arms. Each arm was insulated with a polyethylene tube and mounted with 5 unipolar silver electrodes (0.15 x 4 mm). To avoid injury current, the electrodes were mounted in such a manner that they were not in direct contact with the endocardium. The 8 arms were at equal distance and were connected to each other at both ends so that when the apparatus was expanded, a uniform distribution of electrodes resulted. Two arms were marked with different colours for orientation. The apparatus was 50 mm long and 32 mm across when fully opened. Placement of the apparatus was accomplished by using a thin wall tubing ( inserter) with an outer diameter of 8 mm via the apex. The closed apparatus was placed inside the inserter; a left apical ventriculotomy of approximately 10 mm, simulating the clinical approach, was performed. The inserter was introduced into the apex, and the apparatus placed into the left ventricle.
while withdrawing the inserter. The apparatus was secured by a purse string suture around the point of insertion. The time for positioning the apparatus was a matter of seconds. Once inside the left ventricle, the apparatus deploys, placing the eight arms into position, with each maintaining constant contact with the endocardium. The electrodes were not in direct contact with the endocardium, but they detected the potential changes from the nearest endocardium. These potentials have been compared with those measured by direct contact on the epicardium and found to be identical except for the injury currents observed with the direct contact electrodes. At the end of each experiment, the sheep was sacrificed and the heart opened to verify the positions of the electrodes. The electrode positions corresponded to the tissue samples subsequently taken for measurement of RMBF, so that the ST segment changes after coronary artery occlusion could be correlated with the blood flow of each sample. From the postmortem examination, the distance between the electrodes and the endocardium ranged from 1.3 to 3.0 mm. The apparatus enabled the author to record the signal from a working heart, and to map the whole endocardial surface at one time, although at a moderate spatial resolution. The apparatus removes the difficulties of conventional methods and makes it possible to record the potential while ischemia has been induced with the heart in situ.

Simple hemodynamic measurements in our experiments suggested that the insertion of the 40-pole intracavity electrodes into the left ventricle did not cause significant hemodynamic deterioration. The electrodes did not provoke arrhythmias or injury currents, and they remained in position throughout the experiments. The quality of all unipolar electrical signals remained satisfactory.

The potentials were sampled simultaneously at 1000 samples/sec per channel by a 128 channel data acquisition system directly on to computer memory through an S11W (Engineering Design Team, Inc., 1100 NW Compton, Suite 306, Beaverton, Oregon USA 97006) interface (DMA) to an SBus on a portable computer (BriteLite RDI Computer Corp., 2300 Faraday Avenue, Carlsbad, CA 92008). An immediate display of the sampled electrocardiographic signals enabled a check on the quality of the data. All the potentials were recorded in reference to the left leg. During data acquisition, the opening in the chest wall was covered by warm moist saline pads not in contact with the myocardium. To avoid the interference of injury currents, we obtained recordings at least 20 minutes after the setting up, when the ST-T shifts had disappeared almost completely.

At the termination of each experiment, the sheep was sacrificed and the heart carefully removed from the chest cavity. After marking the epicardial electrode position with mapping pins, the heart was opened and the endocardial electrode positions verified and marked.
By making an incision from the posterior edge to the apex, the ventricles could be opened flat (for endocardial mapping, the incision was made from the middle of the septum). The electrode positions, the epicardial vascular patterns and the outlines of the ventricles were traced onto transparent plastic and transferred to paper, where the coordinates of the whole picture were measured and reconstructed using our own mapping program and the S-Plus statistical package. The picture was then combined with the ST potential contour map to give either an epicardial or an endocardial potential map as illustrated in Figure 1. For each sheep, detailed epicardial potential maps were constructed from the epicardial potentials of the left and the right ventricles. In 10 sheep from groups 2 and 3, detailed endocardial potential maps were also constructed from the endocardial potentials of the left ventricle.

The electrograms were plotted, and their qualities evaluated. Missing or poor electrograms were discarded. Bad leads were picked out and replaced by interpolation from the surrounding leads. The onset of the QRS complex was chosen manually from the plots, and the potentials during a 10 msec portion of the PR segment were averaged for use as a zero-potential reference level. The ST segment maps were each constructed from the data averaged over a 20 msec interval centred on a point 80 msec after the QRS onset. The ST segment potential distributions were displayed as isopotential contour maps in the format shown in Figure 1. Isopotential contours were drawn at 1-2mv intervals using linear interpolation.

Data Analysis and Statistics

The left ventricular pressure, the left atrial pressure and the coronary flows were recorded on a multichannel recorder (Grass Instrument Co., Quiney, Mass., 02169, USA). They were also recorded by a Macintosh II computer via an analogue-to-digital converter (NB-DMA-8, NI-488 for Mac-SN 3643 and Labview software: National Instruments Corporation, 12109 Technology Boulevard, Austin, TX 78727-6204, USA) at a sampling rate of 100Hz. All data points were averaged over at least 40 cardiac cycles and were processed by a SUN workstation (SUN Microsystems, Inc., 2550 Garcia Avenue, Mountain View, CA 94043, USA).

Results were expressed as the mean±SD. Data were analysed by two-tailed Student’s paired t-test with the 0.05 level of probability considered as being significant. Linear correlation were used to analyse the relationship between the myocardial blood flow and the perfusion pressure. Curves for paired data were plotted.

Computer Modelling

Bidomain Model

The myocardium was represented by the bidomain model, in which intracellular and extracellular volumes occupy the same space and were separated everywhere by the membrane.
According to previous studies\(^3\),\(^4\) the intracellular potential \((\Phi_i)\) and the extracellular potential \((\Phi_e)\) are governed by the following equations:

\[
\nabla \cdot \sigma \nabla \Phi_i = \nabla \cdot \sigma_i \nabla \Phi_m
\]

\[
\nabla \cdot \sigma \nabla \Phi_e = -\nabla \cdot \sigma_i \nabla \Phi_m
\]

where \(\sigma = \sigma_i + \sigma_e\) is the bulk conductivity of the heart muscle; the subscripts \(i\) and \(e\) represent the intracellular and extracellular space, respectively and \(\Phi_m\) indicates transmembrane potential. Both spaces are coupled through the transmembrane current where outflow from one region must be equal to inflow to the other. Equation (2) is the governing equation for the extracellular potentials and includes two major components. Firstly, the bioelectric source \((-\nabla \cdot \sigma_i \nabla \Phi_m\)) which is a volume current density \((A/m^3)\), and, secondly, the volume conductor which usually has several compartments with distinct conductivities \((\sigma)\).

The ST segment corresponds to the plateau phase of the action potential. In the normal ECG, the ST segment remains isoelectric because of the zero source (no spatial gradient). When ischemia occurs, the transmembrane potential of injury cells changes, producing non-zero source in the injury boundary which, in turn, gives rise to ST segment shifts.

**Hollow Thick Walled Sphere.**

Consider two concentric spheres as a model of the left ventricle and its surrounding myocardium (figure 2). The inner sphere, of radius \(r_b\), contains the blood mass and the region between the inner sphere and the outer sphere, of radius \(r_a\), represents the cardiac muscle. In terms of a spherical coordinate system \((r, \theta, \phi)\), the blood mass is the region \(0 < r < r_b\) and the myocardium is the region \(r_b < r < r_a\).

Now imagine a region of transmural ischemia which is axially symmetric about the azimuthal axis of the spherical coordinate system, so that the potentials have no \(\phi\) dependence. Further assume that the region of ischemia covers the region \(0 < \theta < \theta_a\) in the myocardium.

Following Tung\(^3\) (chapter 7), the differential equation governing the extracellular potential \(\Phi_e\) in the myocardium is given by

\[
\nabla^2 \Phi_e = -\frac{\sigma_i}{\sigma} (\nabla \cdot M_z)
\]

The right hand side is the Laplacian operator, in spherical coordinates, operating on \(\Phi_e\), with rotational symmetry about the azimuthal angle, ie no \(\phi\) dependence, and is given by
\[ \nabla^2 \Phi_e = \frac{1}{r^2} \frac{\partial}{\partial r} \left( r^2 \frac{\partial \Phi_e}{\partial r} \right) + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial \Phi_e}{\partial \theta} \right) \]

Here, \( \nabla \cdot M_e \) is a dipole layer distributed over the boundary of the ischemic zone, i.e., over the surface defined by \( \theta = \theta_a \) and \( r_b \leq r \leq r_a \). Also, the potential within the blood mass, \( \Phi_b \) is governed by

\[ \nabla^2 \Phi_b = 0 \]

Finally, to completely specify the problem and guarantee a unique solution, a set of boundary conditions is required. Firstly, it is assumed that the whole heart model is sitting in air, so it is effectively insulated, therefore

\[ \text{at} \quad r = r_a, \quad \frac{\partial \Phi_e}{\partial r} = 0 \]

Secondly, at the interface between the muscle and the blood mass there is continuity of extracellular potential and current. Hence

\[ \text{at} \quad r = r_b, \quad \Phi_e = \Phi_b \quad \text{and} \quad \frac{\sigma_e}{\sigma_b} \frac{\partial \Phi_e}{\partial r} = \frac{\partial \Phi_b}{\partial r} \]

where \( \sigma_b \) is the conductivity of blood. Finally, there is a symmetry condition at the centre of the blood mass (so that there is no infinite buildup of potential), giving

\[ \text{at} \quad r = 0, \quad \frac{\partial \Phi_b}{\partial r} = 0 \]

The solution method for the above differential equations is detailed in Tung\(^3\), Chapter 7, and the solution is given as an expansion of Legendre polynomials as

\[ \Phi_e(r, \theta) = \sum_{k=0}^{\infty} \left[ A_k \left( \frac{r}{r_b} \right)^k + B_k \left( \frac{r}{r} \right)^{k+1} + C_k \right] P_k(\cos \theta) \]

and

\[ \Phi_b(r, \theta) = \sum_{k=0}^{\infty} D_k \left( \frac{r}{r_b} \right)^k P_k(\cos \theta) \]

where \( P_k(\cos \theta) \) are the Legendre polynomials. The coefficients \( A_k, B_k, C_k \) and \( D_k \) are given by the following expressions. Firstly,

\[
C_k = \begin{cases} 
\frac{\cos \theta_a - 1}{2} & k = 0 \\
\frac{P_{k+1}(\cos \theta_a) - P_{k-1}(\cos \theta_a)}{2} & k \geq 1 
\end{cases}
\]
assuming a unit strength dipole layer at the ischemic boundary. Also, for \( k = 0 \), \( A_0 = D_0 = C_0 \) and \( B_0 = 0 \) and finally for \( k \geq 1 \)

\[
A_k = -\frac{(k + 1)\sigma_b f_4}{f_1 f_4 - f_2 f_3 (\frac{r_b}{r_a})^{2k+1}} C_k
\]

\[
B_k = \frac{(k + 1)\sigma_b f_2 (\frac{r_b}{r_a})^k}{f_1 f_4 - f_2 f_3 (\frac{r_b}{r_a})^{2k+1}} C_k
\]

\[
D_k = A_k (\frac{r_b}{r_a})^k + B_k
\]

where

\[
f_1 = (k + 1)\sigma_b + k \frac{\sigma}{\sigma_i}
\]

\[
f_2 = -k \frac{\sigma}{\sigma_i}
\]

\[
f_3 = (k + 1)\sigma_b - (k + 1) \frac{\sigma}{\sigma_i}
\]

\[
f_4 = (k + 1) \frac{\sigma}{\sigma_i}
\]

**Isolated Heart Model**

The bidomain equations, particularly equation (2), were also solved in a realistically shaped isolated heart. The geometry of the heart was that of a normal 58-year-old female as was constructed from magnetic resonance imaging scans. It included the atria, ventricles myocardium, parts of the inferior and superior vena cava as well as the pulmonary artery and the aorta.

The finite element method was used to solve equation (2) with the heart represented by a mesh of 60,661 eight-node brick elements, each of size 2x2x2 mm\(^3\). The source was calculated from the width of the ischemic boundary, the given conductivity and the transmembrane potentials and assigned to the corresponding elements. To be able to obtain a unique solution, an inner node was assigned a given potential and to simulate the Wilson central terminal, the mean potential on the epicardium served as a reference potential to present ECG data.

Transmural ischemia was simulated using the above model on both small and large regions of the myocardium. Small ischemic regions were located around the centre of the left ventricular free wall with the ischemic boundary having an octagonal shape through the myocardium. For
the large ischemic regions, transmural ischemia was simulated in both the LAD and LCX territories. Both territories share boundaries at the septum on one side and the lateral region of the left ventricular free wall on the other. In either situation, the ischemic and non-ischemic regions occupy the same volume.

References


Figure 1.
Schematic drawings illustrating our potential recording, map construction, and map display. The left diagram represents the electrode matrix on the front surface of the heart. Distances between electrodes were approximately 5 to 10 mm. The right diagrams depicting epicardial (A) and endocardial (B) contour maps constructed from ST potentials. The schematic drawing of the frames represents the unwrapped epicardial surface of the left ventricle and the right ventricle (A), and the unwrapped endocardial surface of the left ventricle (B). The thick solid lines reflect the coronary arteries. The thin solid and dotted lines indicate ST elevation and ST depression respectively. Numbers inside maps indicate values of voltages in millivolts. Ligated arteries are indicated by bars. All the following contour maps are in this format.

Abbreviations for all figures: LAD: left anterior descending coronary artery LV: left ventricle OM: obtuse marginal branch PDA: posterior descending coronary artery LCX: left circumflex coronary artery RV: right ventricle RMBF: regional myocardial blood flow
Figure 2.
The hollow sphere used for the bidomain model. The angle theta (θ) gives the region of infarction, \( r_a \) the external radius and \( r_b \) the internal radius.